REMARKS

This Amendment is being submitted in response to the non-final Office Action issued by the Office on April 16, 2008, in connection with the above-identified application.

Reconsideration of the above-identified application is respectfully requested in view of the foregoing amendments and following remarks.

STATUS OF ACTION

Claims 23-44 are currently pending in the present application and are subject of the provided response.

In connection with the reply filed by Applicant on July 21, 2007, Applicant traversed the Office's restriction requirement and noted the basis for the removal of the restriction. As a result, the Examiner withdrew the previously issued restriction requirement. Applicant would like to thank the Examiner for withdrawing the restriction requirement. As a result, the currently pending claims are being fully considered in the present application.

Applicant respectfully requests reconsideration of the currently pending claims.

AMENDMENTS TO THE SPECIFICATION

Applicant has amended the Abstract to comply with the guidelines provided. Accordingly, Applicant believes that the amended Abstract is now in compliance with the guidelines set forth in MPEP § 608.01(b). No new matter has been added through the provided amendments. Applicant believes that Office's objection has been overcome and should be withdrawn.

AMENDMENTS TO THE CLAIMS

Applicant has amended Claims 30, 33 and 41 to correct minor typographical errors that were present in the claims as pending. Applicant believes that no new matter has been added through the presenting of these amendments.

REJECTION UNDER 35 U.S.C. SECTION 102

Claims 23-44 are rejected by the Office under 35 U.S.C. Section 102(b) as being anticipated by Schatz (WO 00/75368) (hereinafter the "the '368 reference"). Applicant respectfully traverses this rejection.

The Office states that the '368 reference teaches a method for the manufacture of a nucleic acid molecule as provided and set forth in currently pending claims 23-44. The Office sets forth citations throughout the '368 reference that when combined with one another the

Office suggests anticipate the presently claimed invention. Applicant believes that this combination of steps is misleading and fails to disclose the presently claimed invention.

In particular, the inventors of the present claimed invention even acknowledge and explain the differences between the presently claimed invention and those as provided in the '368 reference starting on the bottom of page 19 of the pending application. As explained, the '368 reference discloses the "Sloning method" wherein the elongated oligonucleotide remains immobilised to a surface, and the donor oligonucleotides are added in the liquid phase of the reaction. As a result, the elongated oligonucleotides are not cleaved from the surface until the final nucleic acid molecule is formed. This is further supported by the disclosure and claims of the '368 reference that specifically provides that in order to obtain an elongated oligonucleotide, the cleavage of the ligation product formed between the first and second oligonucleotide sequences, occurs in the nucleic acid sequence of the second oligonucleotide. Applicant does acknowledge that in one embodiment, cleavage of the ligation product may occur within the first oligonucleotide sequence, but this is disclosed in the embodiment wherein a further oligonucleotide is not coupled to the initial ligation product obtained in coupling the first and second oligonucleotides. Accordingly, the method disclosed in the '386 reference teaches and discloses a method of manufacturing nucleic acid molecules which relies upon the "anchoring" of the elongated oligonucleotide to the solid matrix or surface, such that the elongated oligonucleotide remains immobilised to a surface.

In contrast, the presently claimed invention provides a method wherein the shortened first oligonucleotide and the shortened further oligonucleotides remain immobilised. (See pg. 19 of present application). This is in contrast to the invention disclosed in the '368 reference. As a result, the elongated oligonucleotides are cleaved and may be removed to a new reaction vessel to be combined with a new donor oligonucleotide in solution. This results in a reduction of the variety and number of undesired by-products, this increasing the efficacy of the inventive method for the synthesis of the nucleic acid molecule to be manufactured. (See pg. 19 of the present application).

Applicant notes that the Office suggests that since there is no strict requirement in the claims for a particular order of the steps of the invention, that any reference that teaches all of the steps of the claims, even if in a different order, will be considered to anticipate the claims. Applicant understands the Office's interpretation. As indicated above, Applicant believes that

irrespective of the claim order, the '368 reference actually teaches a different method wherein the ligant product of the oligonucleotides is cleaved by an IIS restriction enzyme such that the extended oligonucleotide continues to be "anchored" to the solid matrix or substrate. Accordingly, the '368 reference does not have those benefits provided for and disclosed in the presently pending application. Such benefits of the presently claimed invention are clearly set forth in the pending application:

> The reason for this improved performance is that the ligation between the first and the second oligonucleotide and the further oligonucleotide and the elongated nucleotide in subsequence rounds of the inventive methods show a higher yield when both oligonucleotides are kept in solution rather than one of them being attached to a surface. Additionally, the reaction kinetics can be better controlled as molarity of the reaction compounds would be changed in subsequent steps by transferring the by-products described above. Typically, the oligonucleotide that provides a part of the nucleic acid molecule to be manufactured by the inventive method, the donor oligonucleotides, i.e. the first oligonucleotide and the further oligonucleotide are present in a new reaction vessel such as a well of a multi-well plate. The reason for this is that by doing so neither the uncleaved ligation product nor the uncleaved donor oligonucleotide which remain immobilised via their modification to a surface, are transferred to a new ligation reaction. This would otherwise result in false ligation products. However, the ligation should occur only between the elongated oligonucleotide and the further at least double-stranded oligonucleotide, which serves again as a donor molecular and provides a further part of the nucleic acid molecule to be manufactured. In addition, the immobilisation step allows that all of the components of the reaction are removed which may be troublesome in subsequent steps.

(See bottom of page 19 to middle of page 20 of present application)

Apart from the above differences, and even if one agrees to the interpretation of the claims as done by the USPTO, the steps as such are not identical in both the instant application and the '368 reference.

The reason therefore is that, as also illustrated in Figs. 1A-1C of the instant application and subject to steps a) –d) of claim 23, the ligation between the first and the second oligonucleotide

occurs in the liquid phase and only subsequently is the ligation product immobilized to a surface (step d). In contrast, the ligation according to the '368 reference occurs with one oligonucleotide already having been immobilized. Accordingly, and irrespective of what the sequence steps is, there is no step disclosed in the '368 reference where both oligonucleotides are actually contained and ligated in the liquid phase.

In view of the provided arguments, Applicant respectfully asserts that '368 reference does not anticipate each and every limitation of the newly presented claimed invention. Moreover, it is clear that the specifically claimed invention provides additional benefits beyond those disclosed in the '368 reference.

Accordingly, Applicant respectfully submits that claims 23-44 are novel and patentable over the '368 reference.

CONCLUSION

Reconsideration of the present application is respectfully requested. Applicants believe that the present application is in condition for allowance. Should the Examiner have any questions concerning the above, or if the Examiner feels that any issues may be expedited by a telephone interview, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

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